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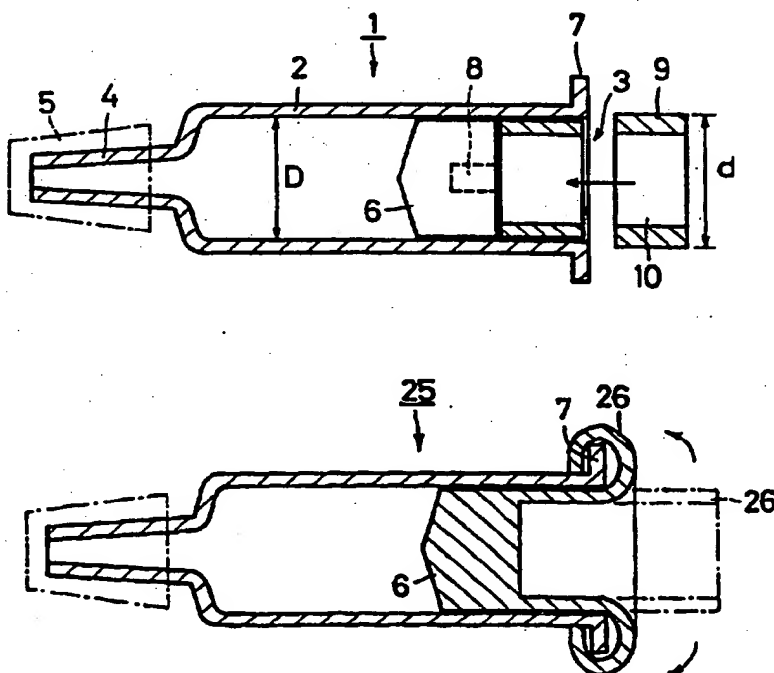
(51) International Patent Classification <sup>6</sup> : A61M 5/28, 5/315, A61J 1/06, A61L 2/06, A61M 5/00		A2	(11) International Publication Number: <b>WO 95/17915</b>
			(43) International Publication Date: 6 July 1995 (06.07.95)
(21) International Application Number: PCT/JP94/02295		(81) Designated States: CA, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, PT, SE).	
(22) International Filing Date: 28 December 1994 (28.12.94)		Published Without international search report and to be republished upon receipt of that report.	
(30) Priority Data: 5/353579 30 December 1993 (30.12.93) JP 6/275690 14 October 1994 (14.10.94) JP 6/338188 27 December 1994 (27.12.94) JP			
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*has piston support means  
but no sleeve*

(54) Title: PREFILLED SYRINGE, TOOLING FOR PREVENTING REMOVAL OF A PISTON FROM THE SYRINGE, AND STERILIZING METHOD USING THE TOOLING

(57) Abstract

The present invention is directed towards eliminating disadvantages of a prefilled syringe (1, 11, 15, 20, 25, 35, 40, 45, 50, 55, 100) including removal of a piston (6, 107) and leakage of a loaded liquid without disturbing the movement of the piston. A prefilled syringe according to the present invention having an outer cylinder (2, 105) which has a nozzle (4) provided in one end thereof and an opening (3, 103) provided in the other end thereof and accommodates therein a piston (6, 107) inserted from the other end, is characterized by a retainer (9, 13) disposed on the other end side of the piston in the outer cylinder (2, 105) for providing a tightness to an inner wall of the outer cylinder. Also, a tooling for preventing removal of the piston according to the present invention is provided comprising a spacer (71) for mounting on the other end side of the piston in the outer cylinder, an other end side retainer plate (72) attached to an other end side of the flange (104) for preventing removal of the piston from the outer cylinder, a one-end side retainer plate (73) attached to a one end side of the flange, and a tightening member (74) for sandwiching and tightening the flange of the prefilled syringe between the other end side retainer plate and the one end side retainer plate.



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**PREFILLED SYRINGE, TOOLING FOR PREVENTING REMOVAL OF A PISTON FROM THE SYRINGE, AND STERILIZING METHOD USING THE TOOLING****TECHNICAL FIELD**

The present invention relates to a means for preventing the removal of a piston or gasket from a prefilled syringe which is caused by increase of the internal pressure of a medical liquid which is loaded in the prefilled syringe.

**BACKGROUND ART**

As shown in Fig. 24, a prefilled syringe 100 comprises an outer cylinder 105 of a tubular shape which is filled with a medical liquid 106 and has a nozzle 102 provided in one end 101 thereof (at left in Fig. 24) and a flange 104 provided in the other end 103 thereof (at right in Fig. 24) where an opening is allocated, a gasket 107 inserted from the opening end 103 into the outer cylinder 105, and a cap 108 fitted onto the nozzle 102. Such prefilled syringes are disclosed in Japanese Utility Patent Unexamined Publications 2-1164 (1990) and 3-9753 (1991) both titling "container syringe". Each of the syringes is filled with a chemical or medical liquid and sealed by a gasket which is made of an elastic material and inserted from an outer cylinder of the syringe.

In common use, the prefilled syringe filled with the medical liquid is heated for sterilization e.g. in an autoclave. During the heating for sterilization, the medical liquid is increased in internal pressure thus causing the gasket to slip out from the outer cylinder of the syringe or leaking between the circumference of the gasket and the inner wall of the outer cylinder. For preventing the removal of the gasket and the leakage of the medical liquid, the gasket of the syringe is particularly arranged in its shape for increasing the tightness to the inner wall of the outer cylinder.

However, when the tightness of the gasket to the inner wall of the outer cylinder is increased, the leakage of the medical liquid and the removal of the gasket from the cylinder may be prevented but a more pressing force shall be needed to drive the gasket for injecting action. This results in inconvenience of the syringe. If the medical liquid in the syringe is a blood vessel contrast medium which is substantially high in the viscosity and volume, the gasket will hardly be driven by fingers thus demanding the use of a highly priced power injector.

It is an object of the present invention to eliminate such substantial

disadvantages of a conventional prefilled syringe as the removal of a gasket and the leakage of a medical liquid without disturbing sliding movement of the gasket.

#### DISCLOSURE OF THE INVENTION

According to the present invention, a prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof and accommodates therein a gasket inserted from the other end is improved in prevention of removal of the gasket by the following arrangement.

As defined in claim 1 of this specification, a prefilled syringe of the present invention is characterized by a retainer disposed on the other-end side of the gasket in the outer cylinder for providing a tightness to an inner wall of the outer cylinder.

As defined in claim 2, it is characterized by a retainer made of an elastic material and arranged integral with an other-end side of the gasket for providing a tightness to an inner wall of the outer cylinder.

As defined in claim 3, it is characterized by a retainer having a stopper portion thereof for releasably engagement with the flange and disposed on the other-end side of the gasket in the outer cylinder.

As defined in claim 4, it is characterized in that the gasket has a stopper portion arranged on an other-end side thereof for releasably engaging with the flange.

As defined in claim 5, the prefilled syringe of the present invention is characterized in that the gasket is made of an elastic material and has a screw pit provided in an other-end side thereof so that it provides a tightness to an inner wall of the outer cylinder when a tapered screw is threaded into the screw pit.

As defined in claim 6, it is characterized in that the outer cylinder is made of an elastic material and has a raised rib(s) formed on the inner wall thereof.

As defined in claim 7, it is characterized in that the outer cylinder has a step recess provided in the inner wall thereof for engagement with a rear or other-end side of the gasket made of an elastic material when assembled.

As defined in claim 8, it is characterized in that the gasket is made of an elastic material and has a cushion portion formed on an one-end side thereof for casing an inner pressure in the outer cylinder.

As defined in claim 9, it is characterized by a retainer having a folding portion thereof for releasably engaging with an outer surface of the outer cylinder and disposed on the other-end side of the gasket.

The prefilled syringe according to any of claims 1 to 9 may be modified in which the outer cylinder has one or more reinforcement ribs formed on an outer surface thereof.

According to the present invention, a tooling for preventing removal of a gasket for use with a prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and a flange formed on the other end thereof, is filled with a medical liquid, and accommodates therein the gasket, the nozzle of the outer cylinder being protected with a cap, is provided comprising: a spacer for mounting on the other-end side of the gasket in the outer cylinder; an other-end side retainer plate attached to an other-end side of the flange for preventing removal of the gasket from the outer cylinder; a one-end side retainer plate attached to a one-end side of the flange; and a tightening member for sandwiching and tightening the flange of the prefilled syringe between the other-end side retainer plate and the one-end side retainer plate.

The tooling may be modified in which the spacer is arranged integral with the other-end side retainer plate or two or more of the spacers are provided. It may also be possible to allow the spacer to be arranged integral with the gasket.

Furthermore, the other-end side retainer plate of the tooling may have an aperture provided therein for accepting the outer cylinder of the prefilled syringe. It is possible to provide two or more of the apertures.

The tightening member of the tooling may be thread means and/or clamp means.

According to the present invention, a method of sterilizing by heat the foregoing prefilled syringe is provided comprising the steps of: disposing the spacer on

the other-end side of the gasket in the outer cylinder; attaching the other-end side retainer plate to the other-end side of the flange and the one-end side retainer plate to the one-end side of the flange; tightening the other-end side retainer plate and the one-end side retainer plate to each other with the tightening member so that the prefilled syringe is coupled to the tooling; and subjecting the prefilled syringe with the tooling to thermal sterilization.

The thermal sterilization of the method may be executed with an autoclave. In the prefilled syringe of the present invention, the displacement of the gasket towards the rear or other-end side of the outer cylinder is prevented by the retainer or its modification. The gasket removal preventing tooling of the present invention is assembled by disposing the spacer on the other-end side of the gasket in the outer cylinder, attaching the other-end side retainer plate to the other-end side of the flange and the one-end side retainer plate to the one-end side of the flange, and tightening the other-end side retainer plate and the one-end side retainer plate to each other with the tightening member so that the prefilled syringe is coupled to the tooling. While the flange of the outer cylinder remains secured between the two retainer plates, the spacer on the other-end side retainer plate is fitted in the outer cylinder of the prefilled syringe thus preventing the gasket from moving towards the other-end side. As the result, the prefilled syringe held by the tooling is free from slipping of the gasket from the outer cylinder caused by increase of the inner pressure of the medical liquid during the heating for sterilization in an autoclave or the like.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a cross sectional view of a prefilled syringe showing an embodiment of the present invention defined in claim 1; Fig. 2 is a cross sectional view of a prefilled syringe showing another embodiment of the present invention defined in claim 2; Fig. 3 is a cross sectional view showing the prefilled syringe of claim 2 with a retainer having a truncated conical shape; Fig. 4 is a cross sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 3; Fig. 5 is a cross sectional view of a prefilled syringe showing a still further embodiment of the present invention defined in claim 4; Fig. 6 is a cross sectional view showing the prefilled syringe of claim 4 with the rear end of a gasket arranged flush with the rear end of an outer cylinder; Fig. 7 is a cross sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 5; Fig. 8 is a cross sectional view showing the prefilled syringe of claim 7 with a tapered screw used; Fig. 9 is a cross

sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 6; Fig. 10 is a cross sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 7; Fig. 11 is a cross sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 8; Fig. 12 is a cross sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 9; Fig. 13 is a cross sectional view of a prefilled syringe showing a further embodiment of the present invention defined in claim 10; Fig. 14 is a perspective view showing a one-end side retainer plate and an other-end side retainer plate in a gasket removal preventing tooling of an embodiment of the present invention; Fig. 15 is a perspective view of a spacer of the gas removal preventing tooling; Fig. 16 is a cross sectional view showing the gas removal preventing tooling to which prefilled syringes are secured; Fig. 17 is a cross sectional view of the gas removal preventing tooling employing a tightening member of thread means; Fig. 18 is a cross sectional view of the gas removal preventing tooling employing a tightening member of clamp means; Fig. 19 is a perspective view showing a number of prefilled syringes assembled with the gasket removal preventing tooling employing the tightening member of thread means; Fig. 20 is a perspective view showing a one-end side retainer plate and an other-end side retainer plate which has a plurality of spacers arranged integral therewith for a gasket removal preventing tooling; Fig. 21 is a cross sectional view showing the gas removal preventing tooling of Fig. 20 to which prefilled syringes are secured; Fig. 22 is a cross sectional view showing a gasket which has a spacer arranged integral with an other-end side thereof; Fig. 23 is a cross sectional view showing a gasket removal preventing tooling for the gasket shown in Fig. 22 to which prefilled syringes are secured; and Fig. 24 is a cross sectional view of a conventional prefilled syringe.

#### BEST MODE FOR CARRYING OUT THE INVENTION

Preferred embodiments of the present invention will be described in more details. Fig. 1 illustrates a prefilled syringe 1 as one of the embodiments of the present invention defined in claim 1 of this application. Similar to Fig. 24, the prefilled syringe 1 comprises an outer cylinder 2 of a tubular shape having a nozzle 4 formed on one end thereof (at left in Fig. 1) and an opening 3 provided in the other end thereof (at right in Fig. 1). While the nozzle 4 is closed with a cap 5, a gasket 6 is inserted into the opening 3 of the outer cylinder 2 so that a medical liquid filled in the prefilled syringe 1 is sealed tightly. In common, the outer cylinder 2 has a flange 7 formed integrally with the outer edge at the other or opening end thereof. The gasket 6 is generally made of an elastic

material such as rubber and has a pit 8 arranged in a rear end thereof at the opening side, which pit 8 can be connected to a handle (plunger). For use of the prefilled syringe 1, after the cap 5 is removed, the nozzle 4 is couple to e.g. a tubing and a handle (plunger), not shown, is introduced from the opening 3 of the outer cylinder 2 and its distal end is threaded into the pit 8 of the gasket 6. When the handle (plunger) is pressed in, the medical liquid flows through the nozzle 4 to the tubing.

The prefilled syringe 1 of this embodiment is characterized by a retainer 9 disposed at the rear end of the gasket 6 as fitted at the other or opening end in the opening 3 of the outer cylinder 2. The retainer 9 is arranged of a ring shape having an outer diameter  $d$  slightly larger than the inner diameter  $D$  of the outer cylinder 2. The retainer 9 is made of a material resistible to thermal sterilization with an autoclave. The material of the retainer 9 may preferably be, but not limited to, an elastic material such as rubber. In use, the retainer 9 is pressed from the opening side into the opening 3 of the outer cylinder 2 and tightly held in the outer cylinder 2 by its elastic strength pressing against the inner wall of the outer cylinder 2, thus preventing the gasket 6 from moving towards the opening end of the outer cylinder 2.

More particularly, if the gasket 6 is urged towards the opening end by an inner pressure of the medical liquid loaded in the outer cylinder 2 of the prefilled syringe 1, its rear end at the opening end remains held with the retainer 9. The gasket 6 is thus prevented from moving towards and slipping from the opening end of the outer cylinder 2. As the result, the prefilled syringe 1 allows the gasket 6 to be securely retained without increasing the tightness between the circumference of the gasket 6 and the inner wall of the outer cylinder 2, avoiding escape of the medical liquid. Also, the ring shape of the retainer 9 permits screwing of the handle into the gasket 6 through an inner space 10 of the retainer 9 for ease of mounting and dismounting of the detachable handle.

Fig. 2 shows a prefilled syringe 11 of another embodiment of the present invention defined in claim 2 of the specification. The prefilled syringe 11 is characterized by a retainer 13 of the elastic material formed integrally with the rear end of a gasket 6. The retainer 13 on the gasket 6 is arranged of a ring shape having an outer diameter slightly larger than the inner diameter of an outer cylinder 2 similar to the previous embodiment shown in Fig. 1. When the ring-shaped retainer 13 has been inserted from an opening end into the outer cylinder 2 as following the gasket 6, it is secured with its elastic strength pressing against the inner wall of the outer cylinder 2



thus preventing the gasket 6 from dislocating towards the opening end of the outer cylinder 2.

Fig. 3 illustrates a modification of the gasket 6 which is made of an elastic material such as rubber and formed integrally with a retainer 16 which has an annular truncated cone shape becoming larger in the outer diameter towards the rear end. In action, the retainer 16 is securely held in the outer cylinder 2 with its elastic strength pressing against the inner wall of the outer cylinder 2, thus preventing removal of the gasket 6 from the outer cylinder 2. When the gasket 6 is pushed at the center by a handle 17 for injecting action, the retainer 16 becomes biased as deflected inwardly radially due to its elasticity. This inward radial deflection allows the gasket 6 to travel along the inner wall of the outer cylinder 2 smoothly in the injecting action.

Fig. 4 shows a prefilled syringe 20 of a further embodiment of the present invention defined in claim 3 of the specification. The prefilled syringe 20 is characterized by a retainer 22 which has a stopper portion 21 thereof for engaging with and disengaging from a flange 7 arranged on the opening end of an outer cylinder 2 and is disposed at the rear end of a gasket 6. The retainer 22 is made of an elastic material, e.g. rubber, and has a tubular shape such that its rear end (i.e. the stopper portion 21) at the opening side is folded outwardly radially to clamp the flange 7 of the outer cylinder 2. As the retainer 22 is secured to the flange 7, it prevents the gasket 6 from displacing towards the opening end of the outer cylinder 2.

Fig. 5 shows a prefilled syringe 25 of a still further embodiment of the present invention defined in claim 4 of the specification. The prefilled syringe 25 is characterized by a gasket 6 having a stopper 26 formed integral with the rear end thereof for engaging with and disengaging from a flange 7 arranged on the opening end of an outer cylinder 2. The stopper 26 is made of an elastic material, e.g. rubber, and has a tubular shape. When a rear end of the stopper 26 at the opening side of the cylinder 2 is folded outwardly radially to clamp the flange 7 of the outer cylinder 2, the gasket 6 is prevented from slipping from the opening end of the outer cylinder 2. In addition, the interior of the outer cylinder 2 is isolated by the clamping of the stopper 26 from the atmosphere and will thus be enhanced in germ-free condition.

Fig. 6 illustrates a modification of the gasket 6, whereas the rear end 31 thereof coincides with the opening end of an outer cylinder 2 while the outer cylinder 2 is filled

with a full volume of the medical liquid. Similar to one shown in Fig. 5, the gasket 6 has a stopper 32 formed on the rear end 31 thereof for engaging with and disengaging from a flange 7 arranged on the opening end of the outer cylinder 2. Accordingly, the gasket 6 is prevented from slipping off and the interior of the outer cylinder 2 is enhanced in the germ-free condition. Also, the gasket 6 can easily be placed at a correct position upon being inserted into the outer cylinder 2.

Figs. 7 and 8 show a prefilled syringe 35 of a further embodiment of the present invention defined in claim 5 of the specification. The prefilled syringe 35 is characterized by a gasket 6 which is made of an elastic material and has a screw pit 8 provided in a rear end thereof for accepting a tapered screw 38. In action, as the tapered screw 38 being screwed in, the gasket 6 becomes expanding radially thus pressing with its circumference against the inner wall of an outer cylinder 2. When the prefilled syringe 35 is heated for sterilization, the gasket 6 of the prefilled syringe 35 remains pressed against the inner wall of the outer cylinder 2 thus being prevented from slipping off. During injecting action of the prefilled syringe 35, the tapered screw 38 is loosened or dismantled to return the gasket 6 from the expanding state to the original state, ensuring the smooth movement of the gasket 6.

Fig. 9 illustrates a prefilled syringe 40 of a further embodiment of the present invention defined in claim 6 of the specification. The prefilled syringe 40 is characterized by a raised rib 41 arranged on the inner wall of an outer cylinder 2. As shown, the raised rib 41 of the outer cylinder 2 is engaged with a recess 43 provided in the circumference of a gasket 6 made of an elastic material in a setting mode. If the gasket 6 is as highly elastic as a rubber, its recess 43 may be eliminated because the rib 41 holds the gasket 6 with equal success. Although this embodiment is not complicated but effective for preventing the removal of the gasket 6, it may be improved by a combination with the means described previously with Figs. 7 and 8. As shown in Fig. 9, the gasket 6 has a screw pit 8 arranged in the rear end thereof so that it can expand outwardly radially with its recess 43 holding the raised rib 41 of the outer cylinder 2 when a tapered screw (not shown) is threaded in the screw pit 8. Accordingly, the engagement between the raised rib 41 and the recess 43 will highly be enhanced thus ensuring no removal of the gasket 6 during the thermal sterilization with an autoclave.

Fig. 10 shows a prefilled syringe 45 of a further embodiment of the present invention defined in claim 7 of the specification. The prefilled syringe 45 is

characterized by a step recess 47 provided in the inner wall of an outer cylinder 2 for engagement with a rear edge of a gasket 6 of an elastic material in a setting mode. In action, the gasket 6 of the prefilled syringe 45 is held with the step recess 49 of the outer cylinder 2 so as not to move towards the opening end of the outer cylinder 2.

Fig. 11 shows a prefilled syringe 50 of a further embodiment of the present invention defined in claim 8 of the specification. The prefilled syringe 50 is characterized by a gasket 6 which is made of an elastic material such as rubber and has a cushion portion 52 formed at the front end thereof by making a front wall of the gasket 6 reduced in the thickness for easing an inner pressure of the medical liquid. In action, when the gasket 6 is urged by the inner pressure, its cushion region 52 retracts as is biased to offset a tension. As the inner pressure exerted on the gasket 6 is eased, the dislocation of the gasket 6 will be prevented.

Fig. 12 illustrates a prefilled syringe 55 of a further embodiment of the present invention defined in claim 9 of the specification. The prefilled syringe 55 is characterized by a retainer 57 which has a folding tab(s) arranged on a rear end thereof for detachably engaging with an external surface of an outer cylinder 2 and is disposed in the rear of a gasket 6. This arrangement is effective even if no flange is provided on the external surface of the opening end of the outer surface 2. It is a good idea to have a pull knob 59 mounted on the rear end of the retainer 57 for ease of removal of the retainer 57.

In any of the prefilled syringes of the prescribed embodiments, it is preferred for compensation that the outer cylinder 2 is reinforced with a reinforcement rib 60 arranged on the circumference of the outer cylinder 2, as shown in Fig. 13. The reinforcement rib 60 may be formed integral with the outer cylinder 2 or provided in the form of an annular separate member mounted to the circumference of the outer cylinder 2. It is also possible to have two or more of the reinforcement ribs 60.

The present invention will now be described in the form of a means for preventing removal of a gasket. The gasket removal preventing means is a tooling provided for use with a common prefilled syringe 100 shown in Fig. 24 which comprises an outer cylinder 105 of a tubular shape filled with a medical liquid 106 and having a nozzle 102 provided in one end 101 thereof (at left in Fig. 24) and a flange 104 provided in the other end 103 thereof (at right in Fig. 24) where an opening is allocated, a

gasket 107 inserted from the other end 103 into the outer cylinder 105, and a cap 108 fitted onto the nozzle 102. The tooling for preventing removal of the gaskets 107 from the syringes 100 comprises a plurality of spacers 71, each disposed on the other end 103 side of the gasket 107 in the outer cylinder 105, an other-end side retainer plate 72 disposed directly on the other end 103 side of the flange 104 for preventing escape of the spacer 71 from the outer cylinder 106, a one-end side retainer plate 73 disposed directly on the one-end 101 side of the flange 104, and tightening means 74 for holding and tightening the flange 104 between the two, one-end side and other-end side, retainer plates 72, 73.

As shown in Fig. 14, the other-end side retainer plate 72 is arranged of a planer sheet and the one-end side retainer plate 73 is also a planer sheet having a number of apertures 75 provided therein. The retainer plates 72 and 73 may be made of, but not limited to, a metal, ceramic, plastic, or resin material. The most preferable material of the retainer plates 72 and 73 is a metal such as SUS316L. The apertures 75 of the one-end side retainer plate 73 have a round shape sized for accepting the outer cylinder 105 prescribed in Fig. 25. More particularly, the outer cylinder 105 of the prefilled syringe 100 is passed through the corresponding aperture 75 of the one-end side retainer plate 73 so that its flange 104 located at the opening or other end 103 is sandwiched between the one-end side retainer plate 73 and the other-end side retainer plate 72, as will be described later.

The spacer 71 is formed of a cylindrical shape as shown in Fig. 15. The height  $h$  and the diameter  $d$  of the spacer 71 may be determined to match the distance  $L$  between the rear end of the gasket 107 and the opening end of the outer cylinder 105 and the inner diameter  $D$  of the outer cylinder 105 in the prefilled syringe 100 shown in Fig. 24. In brief, the spacer 71 is so sized as to be easily inserted and seated on the other end 103 side of the gasket 107 in the outer cylinder 105.

As shown in Fig. 16, the outer cylinders 105 of the prefilled syringes 100 accommodating the gaskets 107 and the spacers 71 located on the other end 103 side of the gaskets 107 are passed through their respective apertures 75 of the one-end side retainer plate 73 until the flanges 104 come into direct contact with the one-end side retainer plate 73 and then, the other-end side retainer plate 72 is attached to other-end 103 sides of the flanges 104. When the one-end and other-end side retainer plates 73, 72 are tightened to each other by the tightening means 74 explained below, the prefilled

syringes 100 are secured in a unit.

The tightening means 74 may comprise thread members as shown in Fig. 17. More specifically, the two retainer plates 72 and 73 are joined to each other by tightening with nuts 79 a set of bolts 78 which extend through holes 76 and 77 provided at given locations in the two retainer plates 73 and 72 respectively. Accordingly, a group of the prefilled syringes 100 are securely held with their flanges 104 tightened between the one-end side retainer plate 73 and the other-end side retainer plate 72 using the bolts 78 and nuts 79. As the result, the displacement of the gaskets 107 towards the other end 103 in the outer cylinders 102 is prevented by their respective spaces 71. The nuts 79 may be eliminated by making threads in either the holes 76 or 77.

The tightening means may be a clamp as shown in Fig. 18. The two retainer plates 73 and 72 holding the flanges 104 of the prefilled syringes 100 therebetween are tightened to each other by a plurality of clamps 80 secured with fastening screws 81.

Fig. 19 is a perspective view showing a group of the prefilled syringes 100 tightly held between the one-end side retainer plate 73 and the other-end side retainer plate 72 by the tightening means 74 of bolts and nuts. While the flange 104 of each prefilled syringe 100 remains held between the two retainer plates 73 and 72, the spacer 71 is securely maintained at place in the outer cylinder 105 thus preventing the displacement of the gasket 107 towards the other end 103 of the outer cylinder 105.

The prefilled syringes 100 arranged in an assembly with the tightening means are heated for sterilization by an autoclave or the like. As the autoclave heats the medical liquid 106 in each outer cylinder 105 to about 120°C to 125°C, the inner pressure in the outer cylinder 105 is increased to a considerable level. Even if the inner pressure in the outer cylinder 105 of the prefilled syringe 100 becomes high, the gasket 107 is securely maintained at its initial location and prevented from displacing towards the other end 103 of the outer cylinder 105.

Fig. 20 illustrates a modification of the other-end side retainer plate 72 which is arranged integral with a number of the spacers 71. More specifically, the spacers 71 on the other-end side retainer plate 72 similar to those shown in Fig. 14 are formed having such a height and a diameter that they are easily inserted and placed at the other end 103 side of the gasket 107 in the outer cylinders 105 of their respective prefilled

syringes 100. Also, a one-end side retainer plate 73 for coupling with the modified other-end side retainer plate 72 has a number of apertures 75 provided in a planer sheet form thereof. The apertures 75 are sized in a round shape for accepting the outer cylinders 105 of the prefilled syringes 100 respectively.

For assembly, when the other-end side retainer plate 72 are attached to the rear or other end 103 sides of the flanges 104 of the prefilled syringes 100 with their spacers 71 inserted to the other end 103 side of the gaskets 107 in the outer cylinders 105, the outer cylinders 105 of the prefilled syringes 100 pass through the corresponding apertures 75 of the one-end side retainer plate 73 and their flanges 104 become at the one end 101 in direct contact with the one-end side retainer plate 73. As the flanges 104 of the prefilled syringes 100 remain held between the two retainer plates 73 and 72 which are tightened to each other by tightening means 74 identical to those shown in Fig. 17 or 19, the prefilled syringes 100 are secured in an assembly.

Fig. 22 shows a gasket 107 arranged integral with a spacer 71 in a prefilled syringe 100. The spacer 71 on the gasket 107 is sized in the height and diameter similar to those shown in Figs. 14 and 21 so that the gasket 107 can be inserted and placed in an outer cylinder 105 of the prefilled syringe 100 without difficulty. Also, a one-end side retainer plate 73 for use with the gasket 107 has a number of apertures 75 provided in a planer sheet thereof as is identical to those shown in Figs. 14 and 21. Similarly, the apertures 75 of the retainer plate 73 are sized in a round shape for accepting the outer cylinders 105 of the prefilled syringes 100 respectively.

For assembly, as the gasket 107 is inserted from the other end 103 into the outer cylinder 105 of the prefilled syringe 100, it is followed by the spacer 71. When the outer cylinders 105 of the prefilled syringes 100 have accommodated the spacers 71 at location therein, they are passed through the corresponding apertures 75 of the one-end side retainer plate 73, as shown in Fig. 23. Simultaneously, an other-end side retainer plate 72 is attached to the other end 103 side of a flange 104 of each the respective outer cylinder 105 so that the one end 101 side of the flange 104 comes into direct contact with the one-end side retainer plate 73. Accordingly, as the flanges 104 of the prefilled syringes 100 are held between the two retainer plates 73 and 72 which are tightened to each other by tightening means 74 identical to those shown in Fig. 17 or 19, the prefilled syringes 100 are secured in an assembly.

### INDUSTRIAL APPLICABILITY

As set forth above, any prefilled syringe of the present invention allows the gasket to be maintained without disturbing its sliding movement thus preventing removal from an outer cylinder or leakage of a loaded liquid.

Also, a gasket removal preventing tooling of the present invention restricts the displacement of gaskets towards the opening side of outer cylinders of the prefilled syringes in case that the inner pressure in the outer cylinders is increased during heating of a loaded liquid for sterilization. Hence, the gasket is assuredly prevented from removing from the outer cylinder.

## CLAIMS

1. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof and accommodates therein a gasket inserted from the other end, characterized by a retainer disposed on the other-end side of the gasket in the outer cylinder for providing a tightness to an inner wall of the outer cylinder.
2. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof, is filled with a medical liquid, and accommodates therein a gasket inserted from the other end, characterized by a retainer made of an elastic material and arranged integral with an other-end side of the gasket for providing a tightness to an inner wall of the outer cylinder.
3. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and a flange formed on the other end thereof where an opening is made, is filled with a medical liquid, and accommodates therein a gasket inserted from the other end, characterized by a retainer having a stopper portion thereof for releasably engagement with the flange and disposed on the other-end side of the gasket in the outer cylinder.
4. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and a flange formed on the other end thereof where an opening is made, is filled with a medical liquid, and accommodates therein a gasket inserted from the other end, characterized by a stopper arranged integral with an other-end side of the gasket for releasably engagement with the flange.
5. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof, is filled with a medical liquid, and accommodates therein a gasket made of an elastic material, having a screw pit provided in an other-end side of the gasket and inserted from the other end, characterized in that the gasket holds fast to an inner wall of the outer cylinder when a tapered screw is threaded into the screw pit.
6. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof, is filled with a medical liquid, and accommodates therein a gasket made of an elastic material and inserted from



the other end, characterized in that the outer cylinder has a raised rib(s) formed on the inner wall thereof.

7. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof, is filled with a medical liquid, and accommodates therein a gasket made of an elastic material and inserted from the other end, characterized in that the outer cylinder has a step recess provided in the inner wall thereof so that a rear or other-end side of the gasket is engaged with the step recess of the outer cylinder.

8. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof, is filled with a medical liquid, and accommodates therein a gasket made of an elastic material and inserted from the other end, characterized in that the gasket has a cushion portion formed on an one-end side of the gasket for easing an inner pressure of the medical liquid.

9. A prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and an opening provided in the other end thereof, is filled with a medical liquid, and accommodates therein a gasket made of an elastic material and inserted from the other end, characterized by a retainer having a folding portion thereof for releasably engaging with an outer surface of the outer cylinder and disposed on the other-end side of the gasket.

10. A prefilled syringe according to any of claims 1 to 9, wherein the outer cylinder has one or more reinforcement ribs formed on an outer surface thereof.

11. A tooling for preventing removal of a gasket for use with a prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and a flange formed on the other end thereof, is filled with a medical liquid, and accommodates therein the gasket, the nozzle of the outer cylinder being protected with a cap, comprising: a spacer for mounting on the other-end side of the gasket in the outer cylinder; an other-end side retainer plate attached to an other-end side of the flange for preventing removal of the gasket from the outer cylinder; an one-end side retainer plate attached to an one-end side of the flange; and a tightening member for sandwiching and tightening the flange of the prefilled syringe between the other-end side retainer plate and the one-end side retainer plate.

12. A tooling for preventing removal of a gasket according to claim 11, wherein the spacer is arranged integral with the other-end side retainer plate.
13. A tooling for preventing removal of a gasket according to claim 11 or 12, wherein two or more of the spacers are provided.
14. A tooling for preventing removal of a gasket according to claim 11, wherein the spacer is arranged integral with the gasket.
15. A tooling for preventing removal of a gasket according to any of claims 11 to 14, wherein the other-end side retainer plate has an aperture provided therein for accepting the outer cylinder of the prefilled syringe.
16. A tooling for preventing removal of a gasket according to claim 15, wherein two or more of the apertures are provided.
17. A tooling for preventing removal of a gasket according to any of claims 11 to 16, wherein the tightening member is thread means and/or clamp means.
18. A method of sterilizing by heat a prefilled syringe having an outer cylinder which has a nozzle provided in one end thereof and a flange formed on the other end thereof, is filled with a medical liquid, and accommodates therein a gasket, the nozzle of the outer cylinder being protected with a cap, with the use of a tooling defined in any of claims 11 to 17, comprising the steps of: disposing the spacer on the other-end side of the gasket in the outer cylinder; attaching the other-end side retainer plate to the other-end side of the flange and the one-end side retainer plate to the one-end side of the flange; tightening the other-end side retainer plate and the one-end side retainer plate to each other with the tightening member so that the prefilled syringe is coupled to the tooling; and subjecting the prefilled syringe with the tooling to thermal sterilization.
19. A method of sterilizing by heat according to claim 18, wherein the thermal sterilization is executed with an autoclave.

FIG. 1

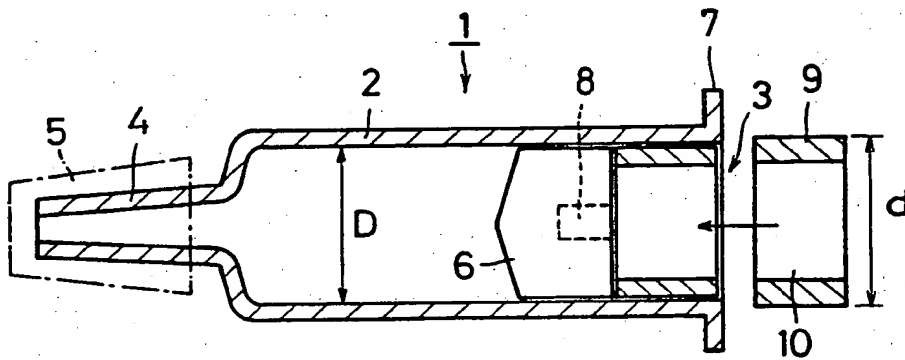


FIG. 2

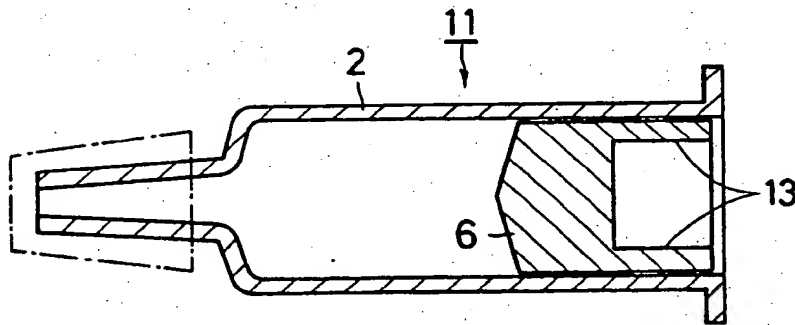


FIG. 3

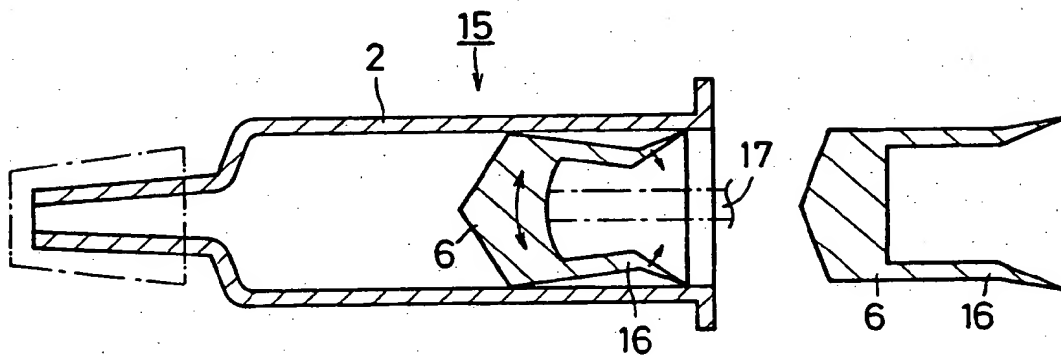


FIG. 4

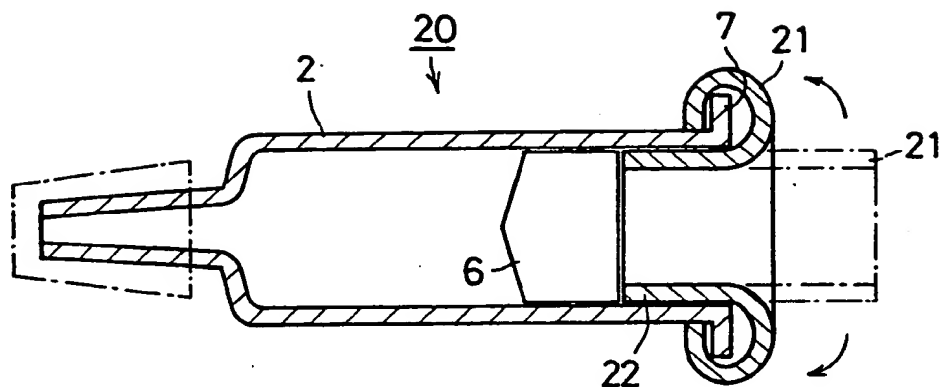


FIG. 5

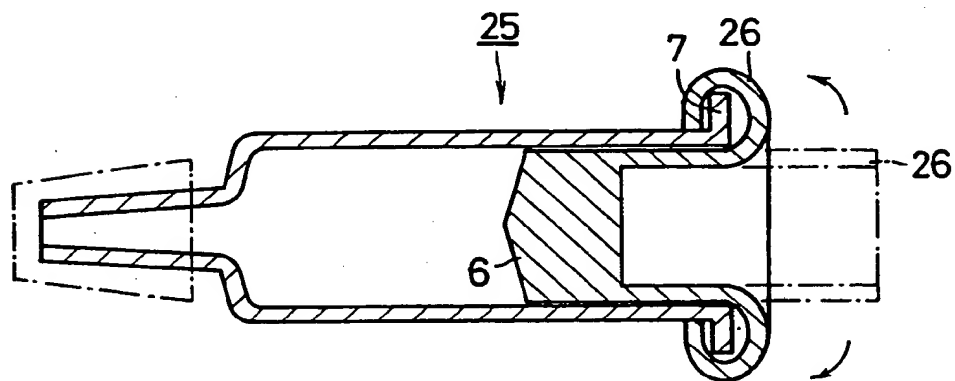


FIG. 6

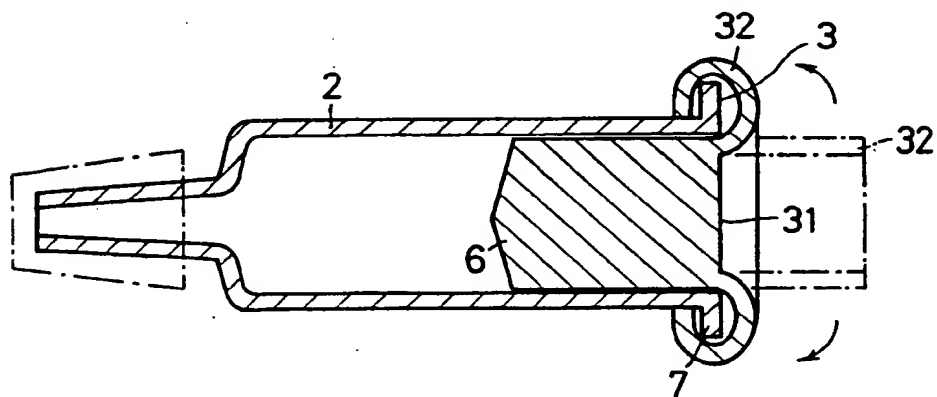


FIG. 7

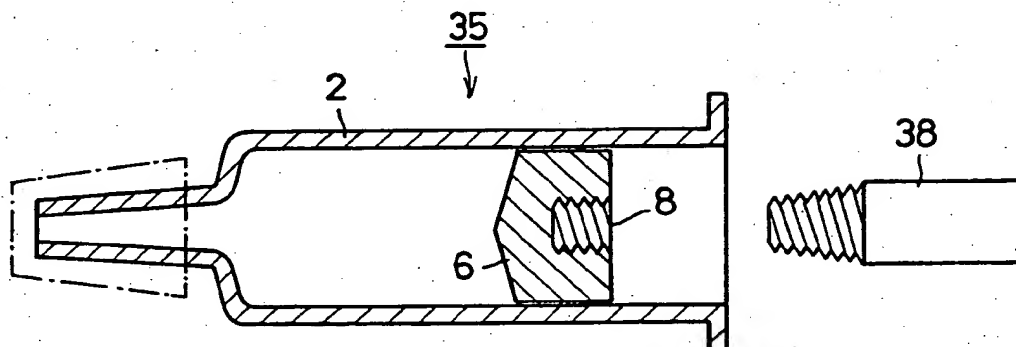


FIG. 8

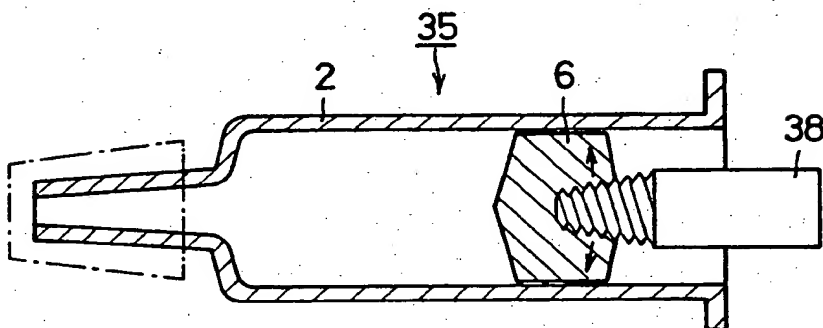


FIG. 9

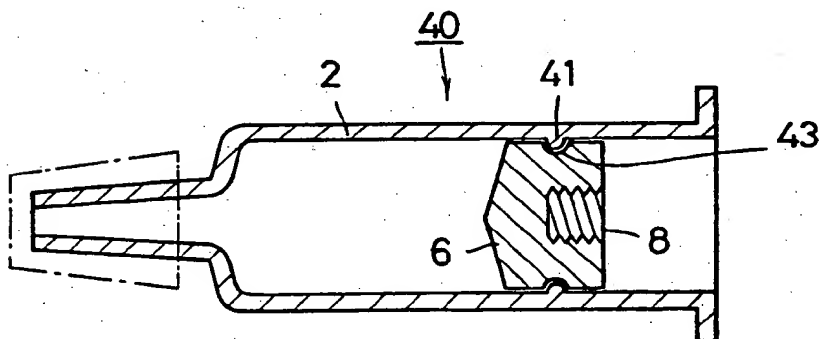


FIG. 10

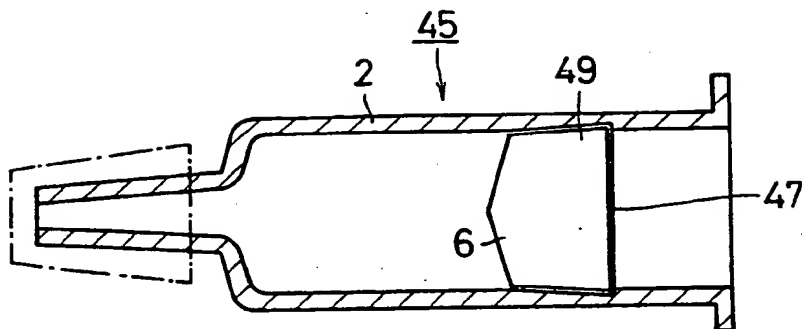


FIG. 11

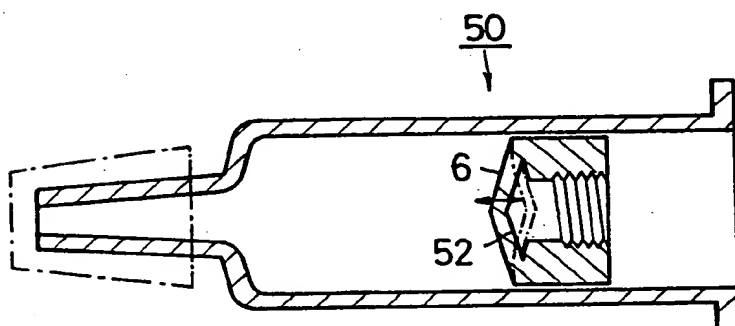


FIG. 12

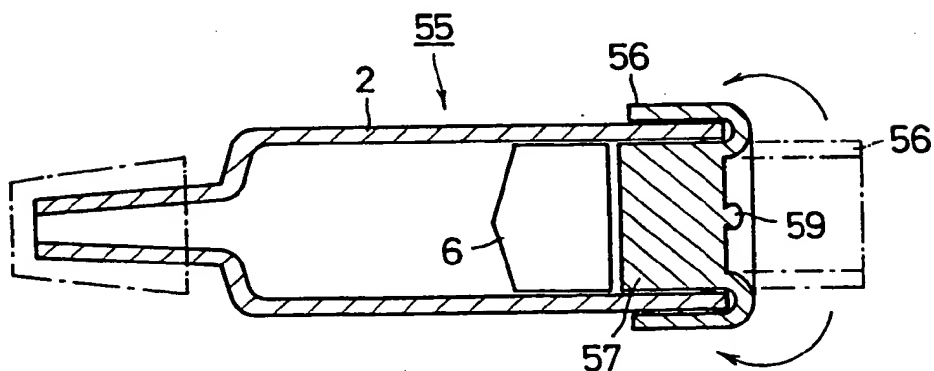


FIG. 13

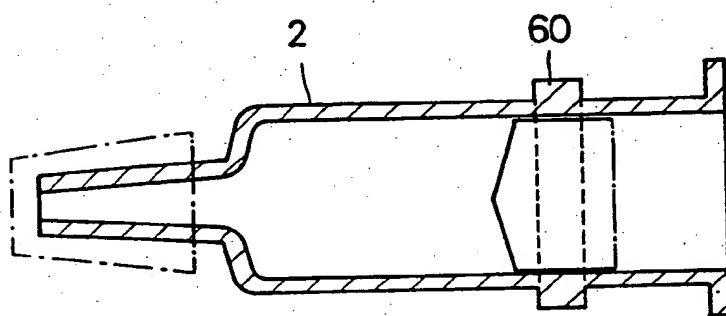


FIG. 14

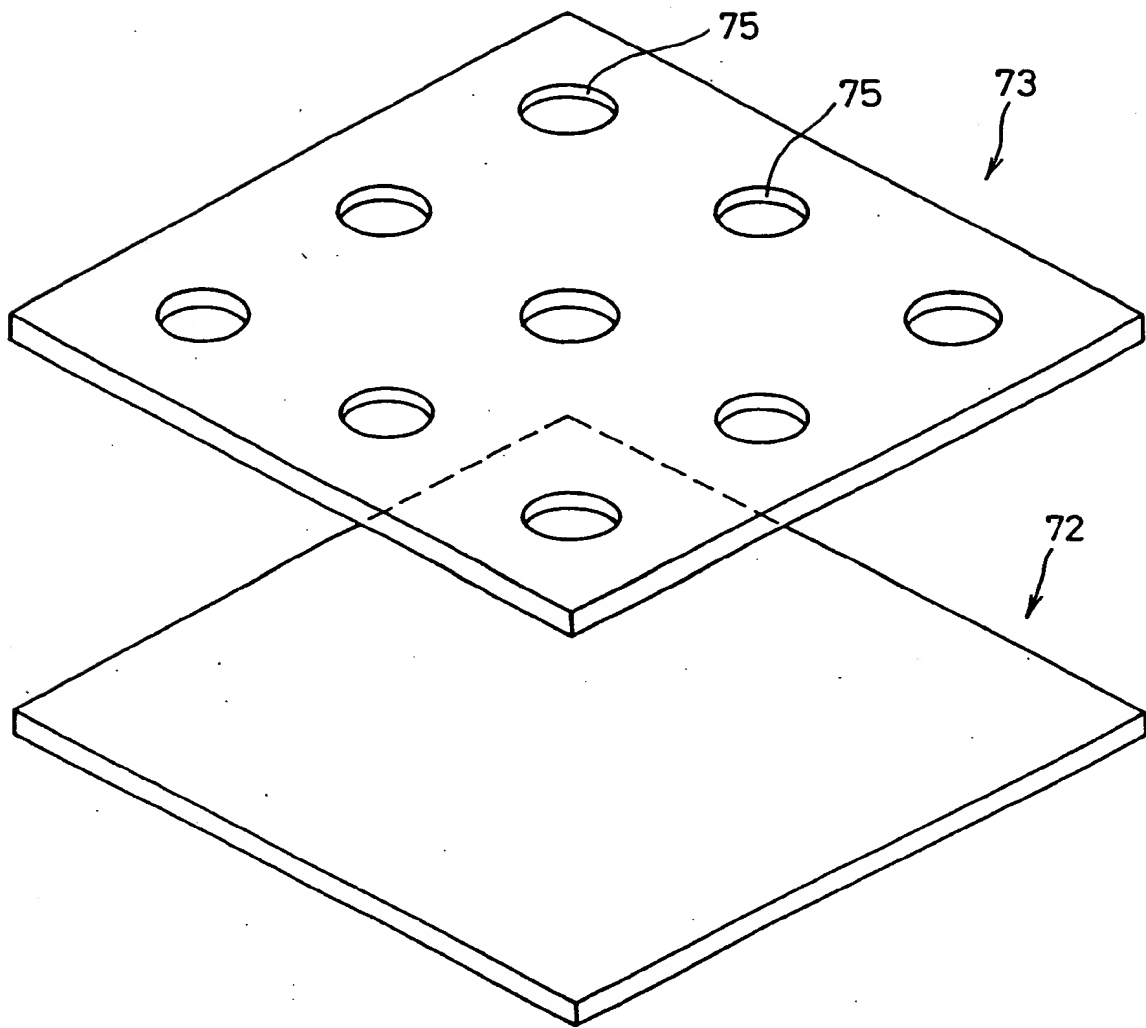


FIG. 15

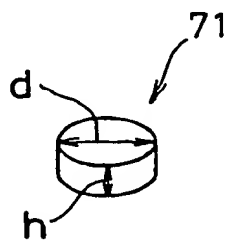




FIG. 16

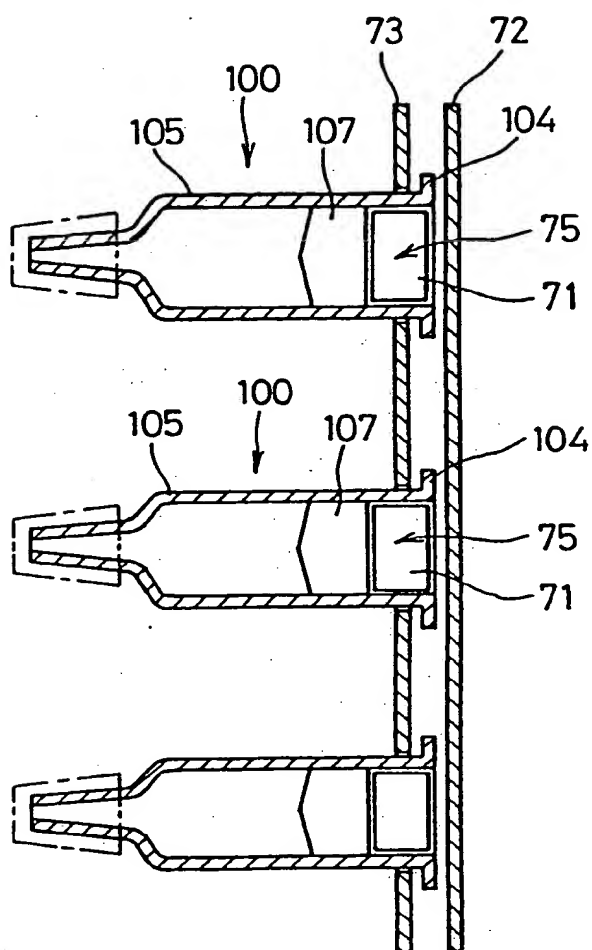


FIG. 17

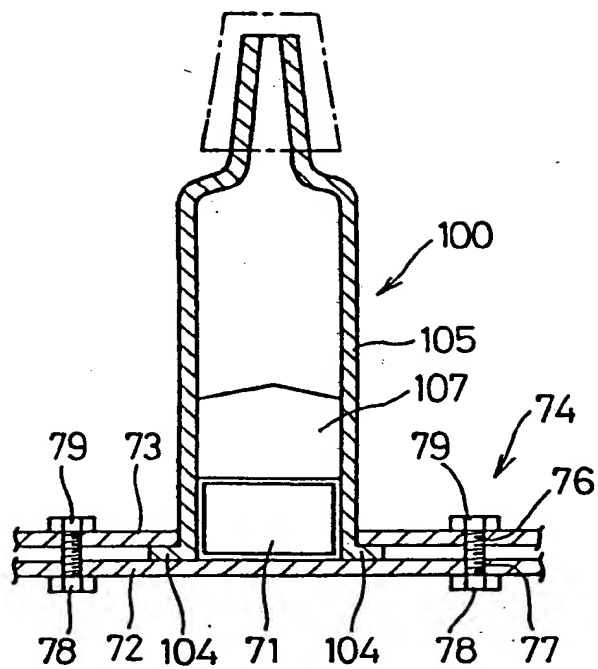


FIG. 18

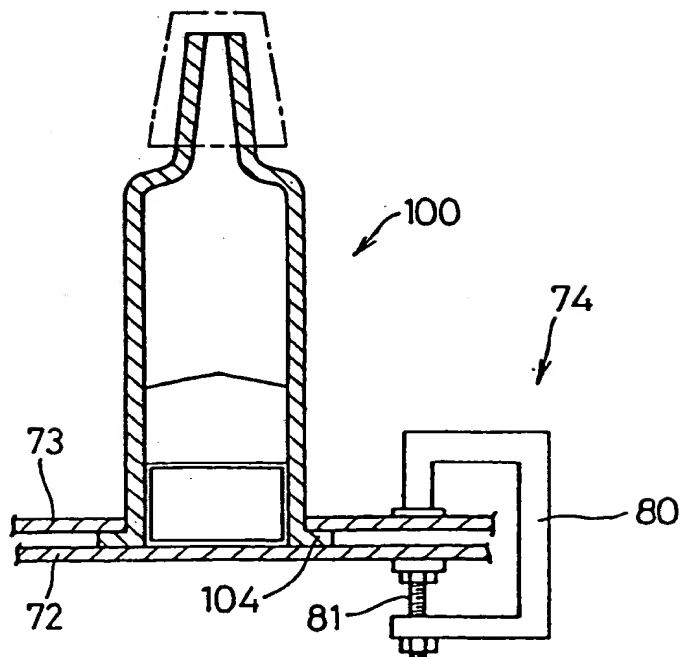


FIG. 19

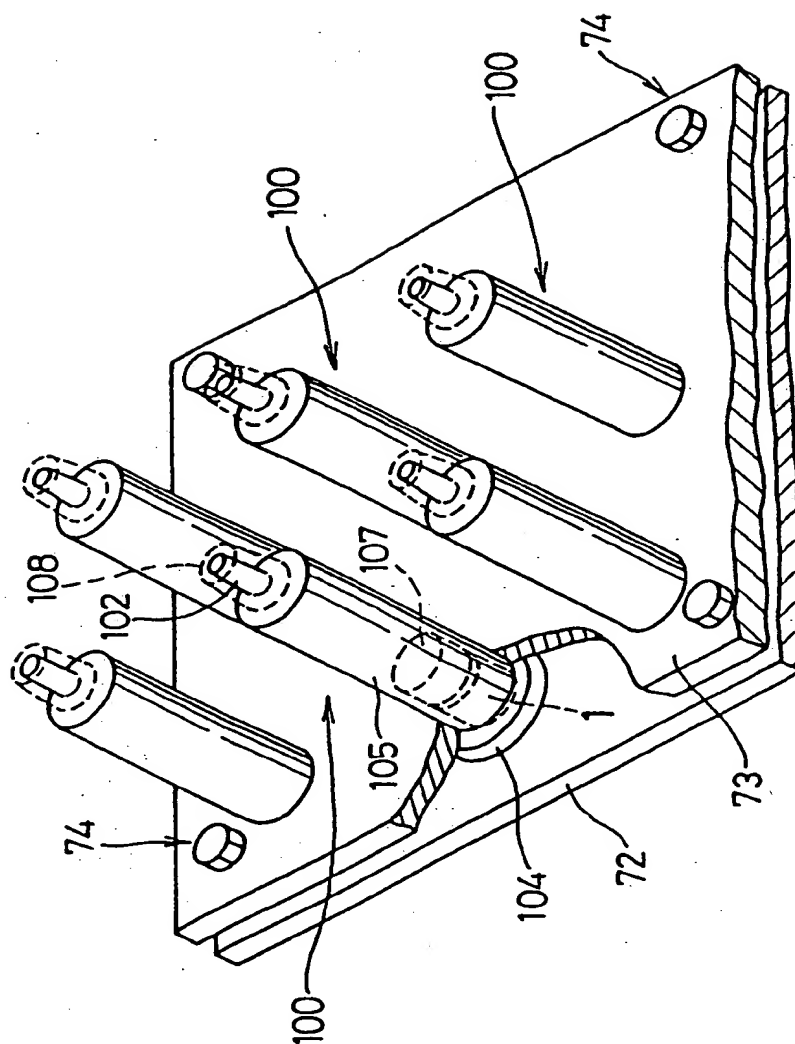


FIG. 20

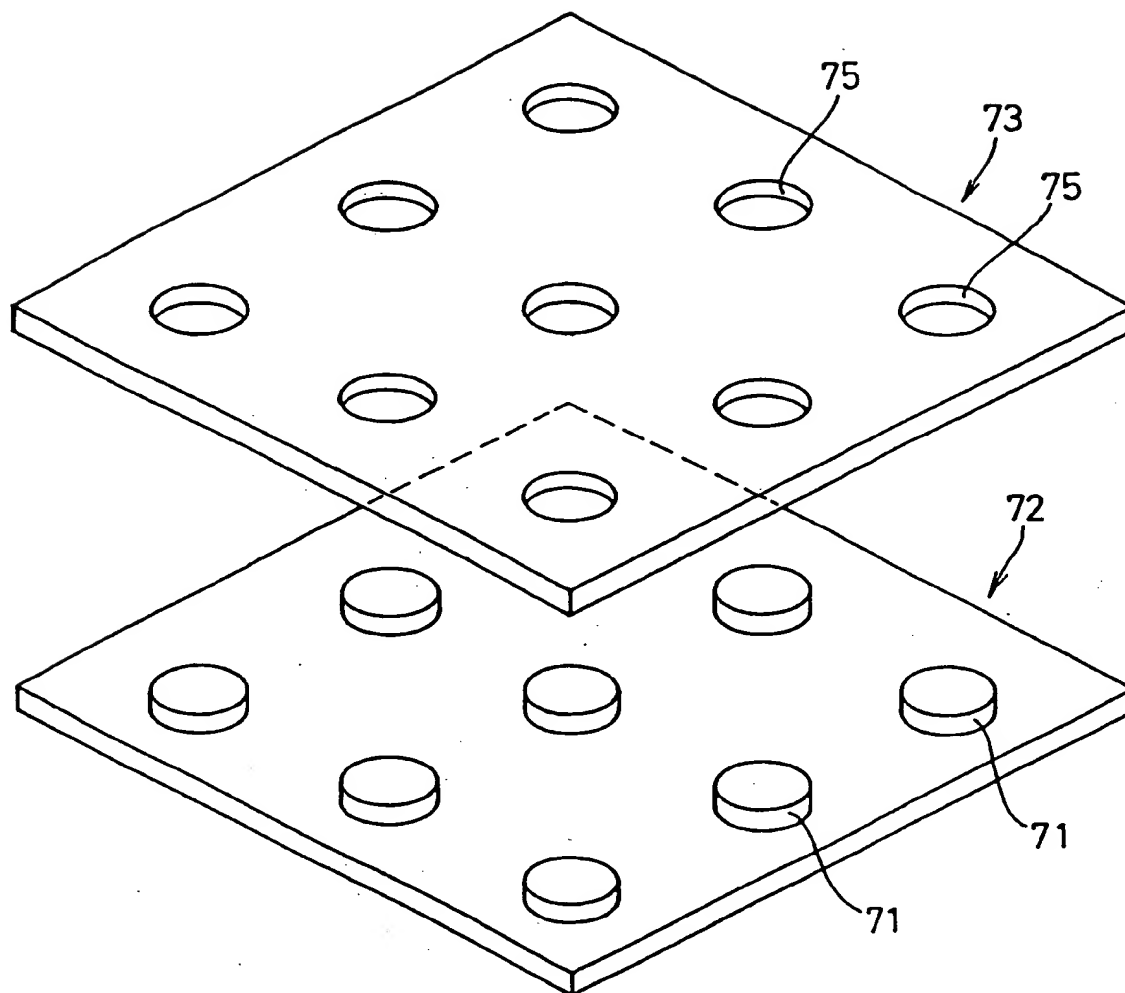


FIG. 21

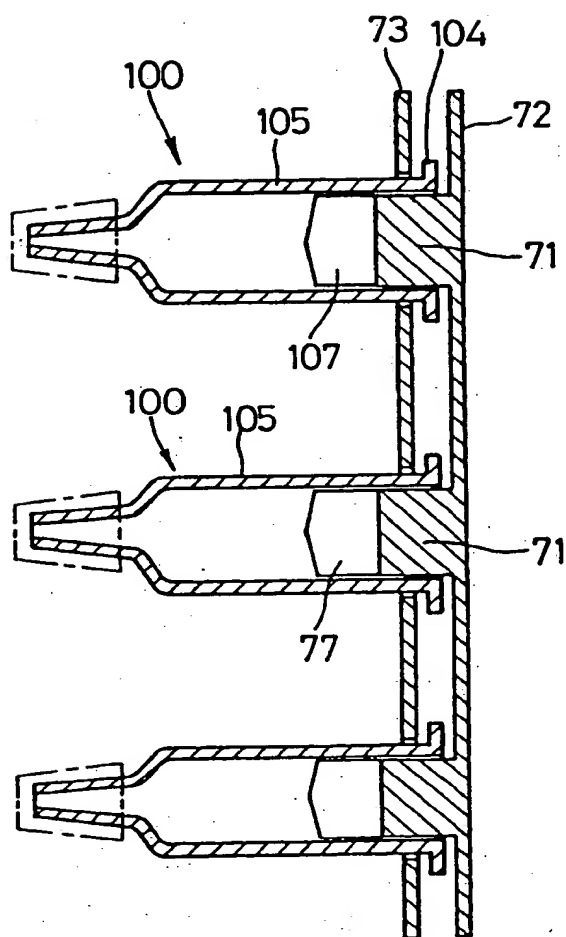


FIG. 22

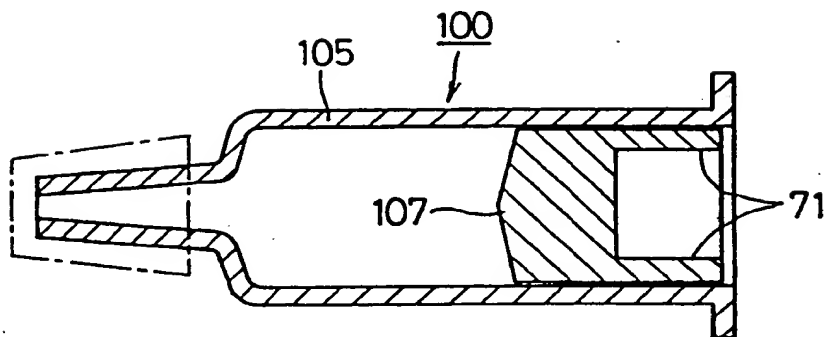


FIG. 23

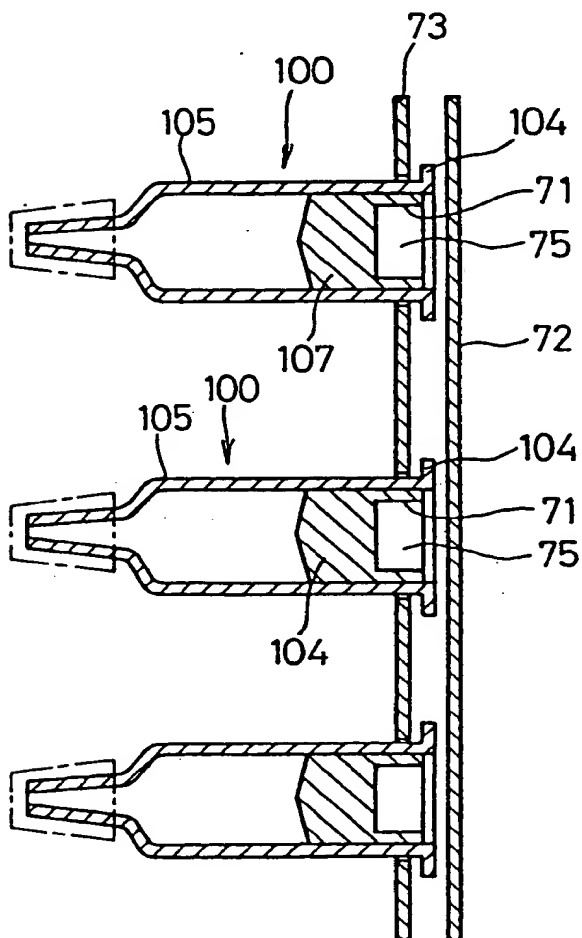
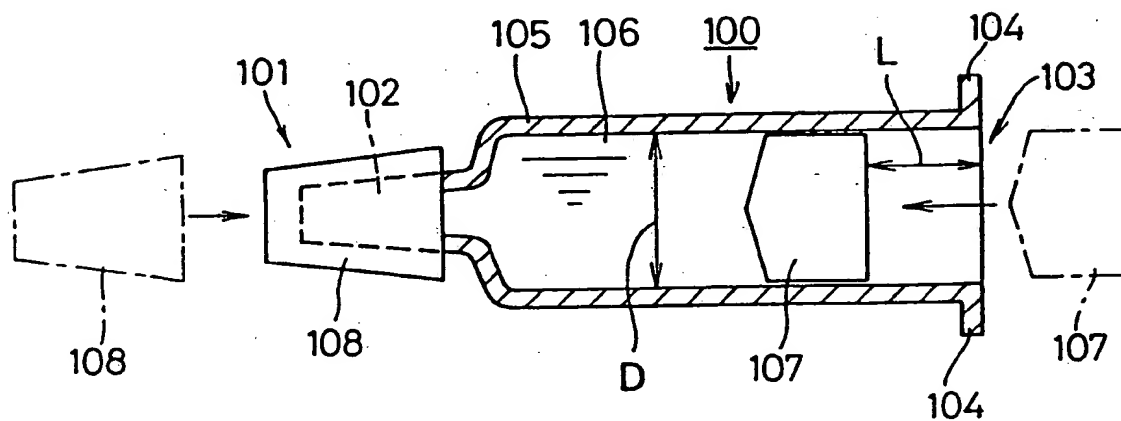


FIG. 24



**Description of Reference Numbers**

- 1, 11, 15, 20, 25, 35, 40, 45, 50, 55, 100: prefilled syringe
- 2,105: outer cylinder
- 3: opening
- 4,102: nozzle
- 5,108: cap
- 6,107: gasket
- 7,104: flange
- 8: screw pit
- 9, 13, 16, 22, 57: retainer
- 21, 26, 32: stopper
- 41: raised rib
- 47: step recess
- 52: cushion portion
- 60: reinforcement rib
- 71: spacer
- 72: an other-end side retainer plate
- 73: a one end side retainer plate
- 74: tightening means



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification<sup>6</sup>:A61M 5/28, 5/315, A61J 1/06, A61L  
2/06

A3

(11) International Publication Number:

WO 95/17915

(43) International Publication Date:

6 July 1995 (06.07.95)

(21) International Application Number: PCT/JP94/02295

(22) International Filing Date: 28 December 1994 (28.12.94)

(30) Priority Data:

5/353579	30 December 1993 (30.12.93)	JP
6/275690	14 October 1994 (14.10.94)	JP
6/338188	27 December 1994 (27.12.94)	JP

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(81) Designated States: CA, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, PT, SE).

## Published

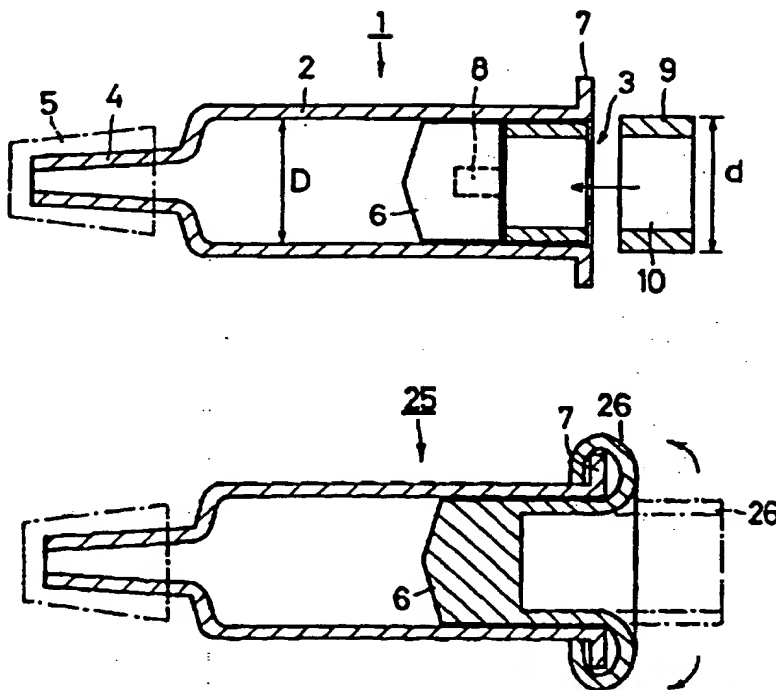
*With international search report.**Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(88) Date of publication of the international search report: 8 September 1995 (08.09.95)

(54) Title: PREFILLED SYRINGE, TOOLING FOR PREVENTING REMOVAL OF A PISTON FROM THE SYRINGE, AND STERILIZING METHOD USING THE TOOLING

## (57) Abstract

The present invention is directed towards eliminating disadvantages of a pre-filled syringe (1, 11, 15, 20, 25, 35, 40, 45, 50, 55, 100) including removal of a piston (6, 107) and leakage of a loaded liquid without disturbing the movement of the piston. A pre-filled syringe according to the present invention having an outer cylinder (2, 105) which has a nozzle (4) provided in one end thereof and an opening (3, 103) provided in the other end thereof and accommodates therein a piston (6, 107) inserted from the other end, is characterized by a retainer (9, 13) disposed on the other end side of the piston in the outer cylinder (2, 105) for providing a tightness to an inner wall of the outer cylinder. Also, a tooling for preventing removal of the piston according to the present invention is provided comprising a spacer (71) for mounting on the other end side of the piston in the outer cylinder, an other end side retainer plate (72) attached to an other end side of the flange (104) for preventing removal of the piston from the outer cylinder, a one end side retainer plate (73) attached to a one end side of the flange, and a tightening member (74) for sandwiching and tightening the flange of the pre-filled syringe between the other end side retainer plate and the one end side retainer plate.



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## INTERNATIONAL SEARCH REPORT

Inter national Application No

PCT/JP 94/02295

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61M5/28 A61M5/315 A61J1/06 A61L2/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61M A61J A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP-A-0 555 900 (STERLING WINTHROP INC.) 18 August 1993 see column 3, line 57 - column 4, line 5 see column 5, line 50 - line 51 see figures 2,6	1,9
Y	---	2,4,10
X	WO-A-92 08507 (DUOJECT MEDICAL SYSTEMS INC.) 29 May 1992 see page 2, line 2 - line 5 see page 9, line 33 - page 10, line 5; figure 5	1
A	---	9
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

26 July 1995

Date of mailing of the international search report

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/JP 94/02295

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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Y	DE-A-24 58 004 (ARZNEIMITTEL GMBH RAVENSBURG APOTHEKER VETTER & CO.) 10 June 1976 see page 11, line 1 - line 13; figure 3	2,4
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X	FR-A-2 353 303 (PHARMA-GUMMI WIMMER WEST G.M.B.H.) 30 December 1977 see page 10, line 21 - line 31; figure 6	8
X	---	
X	FR-A-2 330 412 (LEZARD S.A.) 3 June 1977 see page 2, line 10 - line 12 see figure 2	3,9
Y	---	1,5,7
X	WO-A-92 01485 (NOVO NORDISK) 6 February 1992 see page 4, line 22 - line 26; figures 1,3	6
X	FR-A-2 258 866 (INSTITUT MERIEUX) 22 August 1975 see page 1, line 6 - line 7 see page 3, line 16 - line 30; claims 1,2; figures 1,2	11-13, 15,16, 18,19
Y	---	
Y	US-A-3 987 940 (TISCHLINGER) 26 October 1976 see column 8, line 50 - line 53	10
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Y	---	
Y	DE-A-14 91 834 (PHARMA-GUMMI WIMMER WEST GMBH) 21 August 1969 see page 5, line 13 - line 18; claims 1,2; figures 1,2	7
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A	AU-D-1 440 270 (AB SJUCO) 4 November 1971 see page 5, line 20 - page 6, line 3; figures 1,2	5
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## INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Application No

PCT/JP 94/02295

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-555900	18-08-93	US-A- 5256154	26-10-93
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International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0107874		US-A- 4565543 US-A- 4661098	21-01-86 28-04-87
CH-A-317306		NONE	
DE-A-1491834	21-08-69	NONE	
AU-D-1440270	04-11-71	NONE	

# INTERNATIONAL SEARCH REPORT

ional application No.

PCT/JP 94/02295

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

please see Annex

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

1. Claims: 1-4, 8-10 preventing removal of the piston; integral retaining means
2. Claim: 5 screw thread in an elastic piston, expandable by a tapered screw
3. Claims: 6,7 appropriate shaping on an inner wall of the outer cylinder
4. Claims: 11-19 spacer with means retaining the same in the outer cylinder